

465 INFRAPATELLAR FAT PAD VOLUME AND SIGNAL INTENSITY ALTERATION WERE ASSOCIATED WITH KNEE OSTEOARTHRITIC CHANGES IN PATIENTS WITH KNEE SYMPTOMATIC OSTEOARTHRITIS

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Purpose: Infrapatellar fat pad (IPFP) may play a role in the pathogenesis of knee osteoarthritis (OA) but there is little clinical evidence to support this. The aim of this study was to investigate the associations between IPFP volume, signal intensity alteration and knee structures, including cartilage volume, cartilage defects, bone marrow lesions (BMLs) and radiographic changes in patients with knee OA. The associations between IPFP volume and signal intensity alteration and serum levels of interleukin 17 and adiponectin were also been studied.

Methods: 174 randomly-selected patients with knee symptomatic OA (mean 55.5 years, range 34 to 74, female 85.6%) participated in Anhui Osteoarthritis (AHOA) Study. T1-weighted 3D-SPGR magnetic resonance imaging (MRI) was used to measure the IPFP volume and knee cartilage volume. T2-weighted fat suppressed fast spin echo MRI was utilized to assess knee cartilage defects, bone marrow lesions and IPFP signal intensity changes. Radiographic knee joint space narrowing and osteophytes were assessed using the Osteoarthritis Research Society International atlas. Serum interleukin-17 and adiponectin levels were measured using ELISA.

Results: After adjustment for potential confounders, IPFP volume was significantly and positively associated with knee tibial and patellar cartilage volume (all $p < 0.05$). There were apparently negative associations between IPFP volume and cartilage defects at medial tibial (OR: 0.91, 95%CI 0.84 to 0.98), lateral tibial (OR: 0.90, 95%CI 0.83 to 0.97), medial femoral (OR: 0.88, 95%CI 0.81 to 0.95), lateral femoral (OR: 0.89, 95%CI 0.82 to 0.97) and patellar (OR: 0.90, 95%CI 0.83 to 0.97) sites. Similarly there were significant and negative associations between IPFP volume and bone marrow lesions at lateral tibial (OR: 0.88, 95%CI 0.80 to 0.98) and medial femoral (OR: 0.91, 95%CI 0.83 to 0.99) sites. IPFP volume was also significantly associated with lateral femoral osteophytes (OR: 0.78, 95%CI 0.69 to 0.89). Furthermore, IL-17 was negatively associated with IPFP volume (β : -0.27, 95%CI: -0.46 to -0.08). IPFP signal intensity alteration was significantly associated with lateral tibiofemoral cartilage defect (OR: 1.54, 95% CI: 1.04 to 2.27) and bone marrow lesions at lateral (OR: 1.60, 95% CI: 1.09 to 2.36) and medial (OR: 1.51, 95% CI: 1.03 to 2.21) tibiofemoral compartment. The associations of IPFP signal intensity alteration with lateral (OR: 1.47, 95% CI: 1.00 to 2.16) and medial (OR: 1.69, 95% CI: 1.15 to 2.47) femoral osteophytes were significant. There were distinctly positive associations between IPFP signal intensity alteration and medial tibiofemoral cartilage defects, and lateral and medial tibial osteophytes, but these did not reach statistically significance. Furthermore, there was a negative association between IPFP signal intensity alteration and adiponectin (β : -6.32, 95%CI: -11.84 to -0.81).

Conclusions: This study was the first to report that in patients with knee OA, IPFP volume was negatively associated with knee cartilage volume and positively associated with knee cartilage defects, bone marrow lesions and osteophytes; in contrast, IPFP abnormal quality had opposite associations. These suggest potentially a protective role of IPFP volume and a detrimental role of IPFP abnormal quality in knee OA. Furthermore, interleukin 17 was associated with reduced IPFP volume but adiponectin was associated with decreased abnormal changes of IPFP in knee OA.

466 HYPERCHOLESTEROLEMIA IS A DANGER SIGNAL FOR INCREASING RISK FOR OSTEOARTHRITIS

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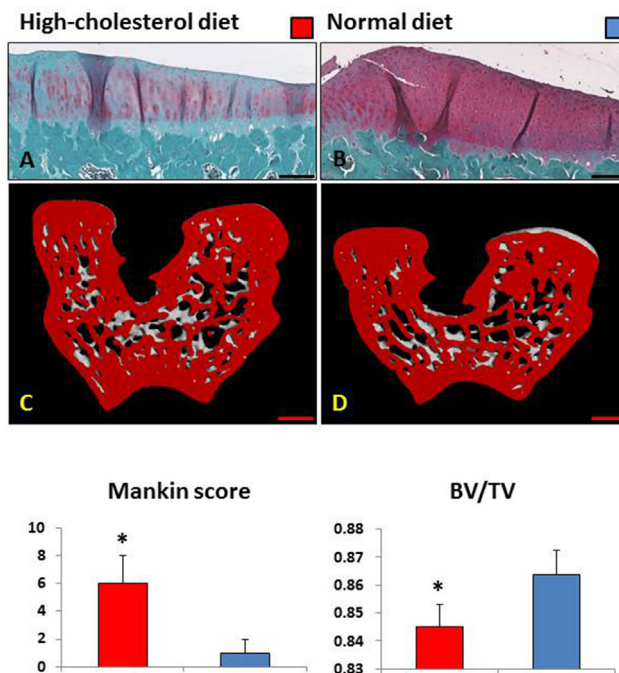
Purpose: Dyslipidaemia is associated with increased risk for developing osteoarthritis (OA); however, the mechanisms implicated are largely unknown. The objectives of this study were to determine whether hypercholesterolemia influences the severity of post-traumatic OA. For this purpose, Apolipoprotein E knockout mice (ApoE^{-/-}) and Wistar rats-both strains which are known to exhibit marked dyslipidaemia

with elevated circulating cholesterol and triglyceride levels-were subjected to a high-cholesterol diet.

Methods: ApoE^{-/-} mice and Wistar rats were fed either normal chow or a high cholesterol diet, starting when the animals were 5 weeks of age. At 8 weeks of age, the destabilization of the medial meniscus (DMM) in the mice and meniscectomy in the rats were performed and used as an experimental OA models. The animals were sacrificed, 4 and 8 weeks after surgery, and effects of hypercholesterolemia on OA disease progression on the knee joints was evaluated by micro-CT scanning to document changes to subchondral bone morphology. Histological sections of the medial tibial plateau, which was divided into inner, middle, and outer regions, were prepared and scored using a modification of the Mankin scoring system. The cartilage thickness was also calculated, and expression levels of aggrecan (ACAN), matrix metalloproteinase 13 (MMP13), and type X collagen (COL10) was assessed by immunohistochemical staining. Moreover, expression levels of mitochondrial damage markers such as cytochrome C, 8 hydroxyguanosine (8OHdG) and malondialdehyde (MDA) were assessed by immunohistochemical staining.

Results: At 8 weeks post-surgery, both ApoE^{-/-} mice and Wistar rats fed with high cholesterol diet showed a number of morphological changes compared with WT mice and rats on control diet: (1) more severe cartilage degeneration in the medial tibial plateau and the femoral condyle; (2) significant reduction of ACAN expression and increased levels of MMP-13 and COL10; (3) reduced bone volume and trabecular thickness in medial tibial subchondral bone (Fig.1). We also observed mitochondrial damage was elevated in the ApoE^{-/-} mice.

Conclusions: The results from this study indicate that hypercholesterolemia increases the risk of symptomatic features of OA and the possible pathway may be via mitochondrial related cell stress.



467 ACTIVIN BA DETERMINES OSTEOPHYTE SIZE IN FEMALE MICE AFTER SURGICAL JOINT DESTABILIZATION

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Purpose: Activin bA is a TGF β family member that is essential for musculoskeletal development. It is strongly regulated upon cartilage injury in vitro (Chong et al, 2003) and surgical joint destabilization in vivo (Burleigh et al, 2012) and is differentially regulated in the secretome of human OA versus normal cartilage (Hermansson et al, 2007). We sought to determine its role in murine disease by inducing OA in a conditional activin bA (Act) knockout mouse.